The ROYAL COLLEGE of OPHTHALMOLOGISTS

www.nature.com/eye

EDITORIAL

Should we still be performing macular laser for non-centre involving diabetic macular oedema? Yes

Eye (2022) 36:483–484; https://doi.org/10.1038/s41433-021-01793-7

Macular laser treatment has been the mainstay treatment of clinically significant diabetic macular oedema (DMO) since the publication of the Early Treatment Diabetic Retinopathy Study (ETDRS) in 1985 [1]. The study showed that macular laser treatment reduces the risk of moderate vision loss by 50% by 3 years. Since randomized controlled trials (RCTs) have demonstrated superior visual outcomes of anti-VEGF injections compared with macular laser treatment, its role in the treatment of DMO has diminished enormously [2–5]. While RCTs were designed to investigate anti-VEGF efficacy, they do not provide answers about the usefulness of macular laser treatment in selected cases. RCTs include patients with centre involving (CI) DMO and central macular thickness above a certain threshold. DMO can present with different phenotypes, and RCTs do not account for morphologic variability. It is well known that focal laser can target leaking microaneurysms located outside the fovea. The RESTORE trial demonstrated that even in focal DMO, which is mostly caused by leaking microaneurysms in contrast to diffuse DMO, in less than 33% of the cases, the leakage was caused by microaneurysms located outside the central subfield, accessible by laser treatment [6]. The DRCR.net Protocol T has clearly shown that even with intensive anti-VEGF therapy under trial conditions, macular laser treatment was still needed in 37–56% of CI-DMO cases during the first year of treatment [7]. Studies investigating non-CI-DMO are lacking. However, as clinicians we see patients with focal extrafoveal DMO which over time encroaches the fovea, reduces vision and the patient finally requires intravitreal treatment [8]. Patients with focal parafoveal oedema benefit from macular laser photocoagulation in terms of anatomical and visual outcome [9]. Moreover, this patient cohort has been shown to have the least response to anti-VEGF therapy [10]. A sub-analysis from the RESTORE trial revealed that macular laser treatment was as effective as anti-VEGF injections in patients with retinal thickness of <300 µm [6]. Hence, patient selection based not on mere macular thickness measurement, but on multimodal imaging findings and disease progression over time is mandatory in order to provide the optimal treatment. The results from DRCR.net protocol V encourage close observation for patients with CI-DMO and preserved visual acuity of ≥20/25 [11]. The results from the OBTAIN real-world study by our study group, the International Retina Group, support these findings [12]. Still, 36.7% of patients with CI-DMO who were observed and not treated experienced visual loss, and further observation led to worse visual outcome. When treatment was initiated after visual decline occurred, some improvement in vision was obtained, but patients still ended up with worse vision at 12 months compared to baseline. This is most probably explained by photoreceptor damage of long-standing macular fluid. Therefore, in patients with non-CI-DMO, macular laser treatment should be considered when encroaching the fovea and endangering vision.

Unlike in clinical trials where eligibility is determined by strict inclusion–exclusion criteria, many people with diabetes in real life have other co-morbidities or are unable to comply with mandatory follow-up visits and miss appointments. Loss to follow-up in patients with DMO was reported in up to 25% of cases during the first year of treatment [13], and subsequent vision loss has been reported [14]. Hence, in non-compliant patients with non-CI-DMO or in patients who cannot afford anti-VEGF or in areas where anti-VEGF therapies are not accessible, macular laser treatment provides a viable treatment option to prevent vision loss.

Early reports raised concerns about macular laser scar enlargement, possible paracentral scotomas, choroidal neovascularization, and subretinal fibrosis when using ETDRS threshold laser [15]. However, with advances in laser technology, these complications are less prevalent. Subthreshold diode micropulse laser (SDM) offers selective treatment targeting the retinal pigment epithelial cells, hereby minimizing collateral tissue damage to overlying photoreceptors and neurosensory retina [16]. SDM has been compared to the ETDRS protocols and found to be equally effective in the treatment of DMO [17]. Focal laser treatment can be performed in a pre-planned safe and precise manner by using image-guided laser systems, such as "Navigated laser (NAVILAS)" [18, 19].

In conclusion, macular laser treatment has its place and is here to stay. It is an efficient and safe treatment. Judicious evaluation of the oedema, disease dynamics and patient compliance need to be taken into consideration.

Dinah Zur[1]✉ and Anat Loewenstein[1]

[1]*Ophthalmology Division, Tel Aviv Sourasky Medical Center, affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel.*

✉*email: dinagz@tlvmc.gov.il*

REFERENCES

1. Early Treatment Diabetic Retinopathy Study Research Group. Photocoagulation for diabetic macular edema. Early Treatment Diabetic Retinopathy Study report number 1. Arch Ophthalmol. 1985;103:1796–806.
2. Rajendram R, Fraser-Bell S, Kaines A, Michaelides M, Hamilton RD, Esposti SD, et al. A 2-year prospective randomized controlled trial of intravitreal bevacizumab or laser therapy (BOLT) in the management of diabetic macular edema: 24-month data: report 3. Arch Ophthalmol. 2012;130:972–9.
3. Elman MJ, Ayala A, Bressler NM, Browning D, Flaxel CJ, Glassman AR, et al. Intravitreal Ranibizumab for diabetic macular edema with prompt versus deferred laser treatment: 5-year randomized trial results. Ophthalmology. 2015;122:375–81.
4. Do DV, Nguyen QD, Boyer D, Schmidt-Erfurth U, Brown DM, Vitti R, et al. One-year outcomes of the da Vinci Study of VEGF Trap-Eye in eyes with diabetic macular edema. Ophthalmology. 2012;119:1658–65.

Received: 19 September 2021 Revised: 23 September 2021 Accepted: 24 September 2021
Published online: 13 October 2021

5. Do DV, Nguyen QD, Khwaja AA, Channa R, Sepah YJ, Sophie R, et al. Ranibizumab for edema of the macula in diabetes study: 3-year outcomes and the need for prolonged frequent treatment. JAMA Ophthalmol. 2013;131:139–45. https://doi.org/10.1001/2013.jamaophthalmol.91.
6. Mitchell P, Bandello F, Schmidt-Erfurth U, Lang GE, Massin P, Schlingemann RO, et al. The RESTORE study: Ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Ophthalmology. 2011;118:615–25. https://doi.org/10.1016/j.ophtha.2011.01.031.
7. Network TDRCR. Aflibercept, bevacizumab, or ranibizumab for diabetic macular edema. N Engl J Med. 2015;372:1193–203. https://doi.org/10.1056/NEJMoa1414264.
8. Vujosevic S, Varano M, Egan C, Sivaprasad S, Menon G, Erginay A, et al. Relevance of retinal thickness changes in the OCT inner and outer rings to predict progression to clinical macular edema: an attempt of composite grading of macular edema. Ophthalmic Res. 2015;55:19–25.
9. Barkmeier AJ, Nicholson BP, Akduman L. Effectiveness of laser photocoagulation in clinically significant macular edema with focal versus diffuse parafoveal thickening on optical coherence tomography. Opthalmic Surg Lasers Imaging. 2009;40:472–9.
10. Allingham MJ, Mukherjee D, Lally EB, Rabbani H, Mettu PS, Cousins SW, et al. A quantitative approach to predict differential effects of anti-VEGF treatment on diffuse and focal leakage in patients with diabetic macular edema: a pilot study. Transl Vis Sci Technol. 2017;6:7.
11. Baker CW, Glassman AR, Beaulieu WT, Antoszyk AN, Browning DJ, Chalam KV, et al. Effect of initial management with aflibercept vs laser photocoagulation vs observation on vision loss among patients with diabetic macular edema involving the center of the macula and good visual acuity: a randomized clinical trial. JAMA 2019;321:1880–94.
12. Busch C, Fraser-Bell S, Zur D, Rodríguez-Valdés PJ, Cebeci Z, Lupidi M, et al. Real-world outcomes of observation and treatment in diabetic macular edema with very good visual acuity: the OBTAIN study. Acta Diabetol. 2019;56:777–84.
13. Best A-L, Fajnkuchen F, Nghiem-Buffet S, Grenet T, Quentel G, Delahaye-Mazza C, et al. Treatment efficacy and compliance in patients with diabetic macular edema treated with ranibizumab in a real-life setting. J Ophthalmol. 2018;2018:4610129.
14. Matsunaga D, Wu CM, Obeid A, Wibbelsman TD, Hsu J. Visual outcomes in eyes lost to follow up with diabetic macular edema treated with anti-vascular endothelial growth factor. Invest Ophthalmol Vis Sci. 2020;61:4878.
15. Schatz H, Madeira D, McDonald HR, Johnson RN. Progressive enlargement of laser scars following grid laser photocoagulation for diffuse diabetic macular edema. Arch Ophthalmol (Chic, Ill 1960). 1991;109:1549–51.
16. Sivaprasad S, Elagouz M, McHugh D, Shona O, Dorin G. Micropulsed diode laser therapy: evolution and clinical applications. Surv Ophthalmol. 2010;55:516–30. https://www.sciencedirect.com/science/article/pii/S0039625710000433.
17. Figueira J, Khan J, Nunes S, Sivaprasad S, Rosa A, de Abreu JF, et al. Prospective randomised controlled trial comparing sub-threshold micropulse diode laser photocoagulation and conventional green laser for clinically significant diabetic macular oedema. Br J Ophthalmol. 2009;93:1341–44. http://bjo.bmj.com/content/93/10/1341.abstract.
18. Kozak I, Oster SF, Cortes MA, Dowell D, Hartmann K, Kim JS, et al. Clinical evaluation and treatment accuracy in diabetic macular edema using navigated laser photocoagulator NAVILAS. Ophthalmology 2011;118:1119–24.
19. Kernt M, Cheuteu R, Vounotrypidis E, Haritoglou C, Kampik A, Ulbig MW, et al. Focal and panretinal photocoagulation with a navigated laser (NAVILAS®). Acta Ophthalmol. 2011;89:e662–4.

FUNDING INFORMATION

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

Correspondence and requests for materials should be addressed to Dinah Zur.